UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/511,205 | 02/15/2005 | Michael Cahill | 26418U | 6456 |

20529 7590 10/26/2006

NATH & ASSOCIATES
112 South West Street
Alexandria, VA 22314

| EXAMINER | |
|---|---|
| AEDER, SEAN E | |
| ART UNIT | PAPER NUMBER |
| 1642 | |

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/511,205 | CAHILL ET AL. | |
| | Examiner | Art Unit | |
| | Sean E. Aeder, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *24-51* is/are pending in the application.

4a) Of the above claim(s) *24,26-44,47 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,45,46,48,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***Detailed Action***

The Election filed 8/22/06 in response to the Office Action of 2/23/06 is acknowledged and has been entered. Applicant elected group II and the species "polypeptide", "intravenous", and "inhibitors" with traverse.

The traversal is on the ground(s) that the claims of group II and the claims of group III possess "unity of invention" because they share a special technical feature as required by PCT Rule 13.2. Applicant states that the special technical feature that is shared between group II and group II is the "diagnostic reagent". Applicant further argues that the election of species of "substance or active ingredient" (a-c) is not essential. Applicant states that one of skill in the art would recognize that specific molecules differentiated in the species, can be generated, designed, selected, or otherwise obtained to bind with high affinity and specificity to any diagnostic target. Applicant further states that it would follow that having discovered the diagnostic value of any particular protein, all the methods of detection of that protein would be known to the person who discovered the diagnostic value. Applicant further argues that the election of species of "mode of administration" (d-g) is not essential. Applicant states that there are a number of possible routes of administration for the reagent of the present invention and restriction to a single one is unnecessary and is contrary to the principals of patent law in general. Applicant further states that complications and legal grey zones created by such a restriction make it improper. Applicant further states that species (h)-(k) share similar function and examination of (h)-(k) does not cause any serious burden on the Examiner. Applicant further states that any restriction of the

claims based on the groups and the species suggested by the Examiner would place an undue burden upon the Applicants with regard to commercialization of the invention. Applicant further states that as all of the groups and the species are closely related, any intellectual property right stemming from this application should issue concurrently. Applicant further argues that the requirement omits "an appropriate explanation" as to the existence of a "serious burden" if a restriction were not required (see MPEP 803). Applicant further argues that the Examiner has powerful electronic search engines that would quickly and easily search all of the claims. Applicant further states that the Examiner will most likely undertake a search for the power plant of claim 34 and searching for the power plant of other independent claims would be minimally burdensome. Applicant further sates that given the overlapping subject matter and identical classification of the species, examinations of all the invention groups would not pose a serious burden because they would be coextensive. Applicant further states that the classification system at the USPTO is based in part upon administrative concerns and is not necessarily indicative of separate inventive subject matter in all cases. Applicant further states that if Examiner refuses to examine all claims filed with the instant application and persists in requiring applicants to file divisional applications for each of the groups of claims, the Examiner would essentially be forcing applicants to pay duplicative fees for the non-elected or withdrawn claims.

The arguments filed in the Election of 8/22/06 have been carefully considered, but are not found persuasive. The Restriction Requirement of 2/23/06 is in compliance with PCT Ruses 13.1, 13.2, and PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b)

and (d). A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. When claims to different categories are present in the application, the claims will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) A product and a process specially adapted for the manufacture of said product; or (2) A product and a process of use of said product; or (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or (4) A process and an apparatus or means specifically designed for carrying out the said process; or (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process. The allowed combinations do not include multiple products and multiple methods of using said products, as claimed in the instant application. The products themselves do not share significant structural elements to the extent that each member could be substituted, one for the other, with the expectation that the same intended results would be achieved. For example, polynucleotide sequences comprise significant differences in chemical compositions and lengths which, in turn, encode a multitude of amino acids with different chemical compositions and lengths all of which would have different molecular weights, specificities, and biological activities. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application is considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). Group 1 is the main invention. After that, all other products and methods are broken

out as separate groups (see 37 CFR 1.475(d).). In the instant case, the first invention of the first category mentioned consists of a method for prevention or treatment of tumors of prostatic carcinomas and the first recited invention of a product to be used with said method is a pharmaceutical agent which influences the expression or function of proteins synthesized or secreted by tumors. It is noted that there is no recited "process of manufacture" of said product. Therefore, a method for prevention or treatment of tumors of prostatic carcinomas and a pharmaceutical agent which influences the expression or function of proteins synthesized or secreted by tumors is considered the "main invention" and the remaining products and methods have been properly restricted into separate groups. Further, it is noted that species of (a)-(c) and the species of (h)-(k) do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The species represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. Further, it is noted that the species of (d)-(g) do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The methods of the above species differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success such that one species could not be interchanged with the other. Further, in regards to the traversal that the examination of all groups would not impose a serious burden on

the examiner, these arguments have been considered but are not found persuasive as such arguments do not apply when restriction is required under 35 USC 121 and 372, as in the instantly filed application. Thus, when the Office considers international applications as an International Searching Authority, as an International Preliminary Examining Authority, and during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 24-51 are pending.

Claims 24, 26-44, 47, and 49 are withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 25, 45, 46, 48, 50, and 51 are currently under consideration.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45, 46, 48, and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 45, 46, 48, and 51 are rejected for reciting the term "active ingredient". There is insufficient antecedent basis for this limitation in the claims.

Claims 45 and 46 are rejected for reciting: "...the substance is directed against". It is not clear from the claims or the specification what is meant by "directed against". This renders the claim indefinite because the term "directed against" is not defined by the claim and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear whether "directed against" means "specifically bind", "specifically inhibits", and/or something else. Given the above reasons, the metes and bounds of the claims cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 45, 46, 48, 50, and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of peptides which detect the expression of or the function of proteins synthesized or secreted by tumors (see claim 25), a genus of peptides directed against proteins synthesized or secreted by tumors (see claim 45, in

particular), peptides directed against inhibitors of proteins synthesized or secreted by tumors (see claim 46, in particular), a genus of peptides that preferably influence, in particular inhibit, the expression or function of proteins synthesized or secreted by tumors (see claim 48, in particular). However, the written description only reasonably conveys peptides comprising antibody fragments that specifically bind proteins listed in table 1. The specification does not disclose any other peptides directed against any other proteins synthesized or secreted by tumors. Further, the specification does not disclose any peptides that would detect the *function* of any protein. Further, the specification does not disclose any peptides that would function *in vivo* as an inhibitor of the expression of or function of any proteins synthesized or secreted by tumors. Further, the specification does not disclose any peptides directed against inhibitors of proteins synthesized or secreted by tumors. Further, the specification does not disclose any inhibitors of proteins synthesized or secreted by tumors.

The specification states that the proteins synthesized and/or secreted by the tumors may be the proteins listed in table 1 and the substances employed for detecting and/or for diagnosing tumor-associated disorders may be an antibody directed against said proteins (see paragraph 16, in particular). A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative

number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of peptides that encompass the genera nor does it provide a description of structural features that are common to said peptides. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of the peptides listed in Table 1 is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the

encompassed genera, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only peptides comprising antibody fragments that specifically bind proteins listed in table 1, and are only characterized by their ability to specifically bind proteins listed in table 1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 25, 45, 46, 48, 50, and 51 are rejected under 35 U.S.C. 112, first paragraph, because, while the prior art is enabling for a method for diagnosing apoptotic cell death associated with lymphoma tumors, wherein lymphoma cells are brought into contact with an Annexin V peptide which detects phosphatidylserine residues due to the pro-apoptotic function of proteins synthesized by lymphoma tumors (see Blankenberg et

al, PNAS, 5/98, 95: 6349-6354), the specification does not reasonably provide enablement for a method for diagnosing just any disorder associated with just any type of tumor by contacting eukaryotic cells with just any peptide which detects the expression or function of just any protein synthesized or secreted by tumors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are drawn to in vitro and in vivo methods for diagnosing just any disorder associated with just any type of tumor by contacting eukaryotic cells with just any peptide which detects the expression or function of just any protein synthesized or secreted by tumors.

The specification states that the proteins synthesized and/or secreted by the tumors may be the proteins listed in table 1 and the substances employed for detecting and/or for diagnosing tumor-associated disorders may be an antibody directed against said proteins (see paragraph 16, in particular).

The state of the prior art dictates that if a molecule is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the molecule to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be

confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the molecule's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the molecule in any diagnostic setting without undue experimentation.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to in vitro and in vivo methods for diagnosing just any disorder associated with just any type of tumor by contacting eukaryotic cells with just any peptide which detects the expression or function of just any protein synthesized or secreted by tumors, and Applicant has not enabled said method because it has not been shown that just any peptide which detects the expression or function of just any protein synthesized or secreted by tumors would predictably diagnose every disorder associated with every type of tumor. The level of unpredictability for the detection of any disease or disorder associated with any type of tumor is quite high. Experimentation to determine whether peptides which detect the expression or function of every protein synthesized or secreted by tumors would predictably diagnose every possible disorder associated with every tumor would in itself be inventive.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25, 45, 46, 48, and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Blankenberg et al (PNAS, 5/98, 95: 6349-6354).

Claims 25 and 48 are drawn to a method for diagnosing disorders associated with tumors, wherein eukaryotic cells are brought into contact with a peptide which detects the expression or function of proteins synthesized or secreted by tumors. Claim 45 is drawn to the method of claim 25, wherein the peptide is directed against the proteins synthesized or secreted by tumors. Claim 48 is drawn to the method of claim 25, wherein the peptide is directed against inhibitors. Claim 51 is drawn to the method of claim 25, wherein the peptide "can" be administered intravenously.

Blankenberg et al teaches a method for diagnosing apoptotic cell death associated with tumors, wherein eukaryotic cells are brought into contact with an Annexin V peptide which detects the pro-apoptotic function of proteins synthesized by tumors (see pages 6352-6353, in particular). Thus, the Annexin V peptide of the method of Blankenberg et al is broadly "directed against" the pro-apoptotic proteins synthesized by tumors. Blankenberg et al further teaches the Annexin V peptide is detects phosphatidylserine (page 6349, in particular). The specification further teaches the presence of phosphatidylserine is indicative of apoptosis and disease progression

(page 6349, in particular). One of skill in the art would recognize that progression of disease leads to the inhibition of health. Therefore, the Annexin V peptides taught by Blankenberg et al are directed against inhibitors of health. Further, although Blankenberg et al teaches intraperitoneal injection of the Annexin V peptide, one of skill in the art would recognize that the Annexin V peptide could be administered intravenously.

***Summary***

No claim is allowed. Claim 50 is rejected under 35 U.S.C. 112, first paragraph, but free of the prior art teaching a method for diagnosing disorders associated with prostate cancer tumors wherein eukaryotic cells are brought into contact with a peptide which detects the expression or function of protein synthesized or secreted by tumors. The closest prior art for claim 50 is Cher and Carroll (1995, West J Med, 162:235-242), which teaches a method of diagnosing prostate cancer wherein serum is brought into contact with antibodies specific for PSA (page 238, in particular); however, this reference does not teach or suggest a method for diagnosing *disorders associated with prostate* cancer tumors wherein *eukaryotic cells* are brought into contact with a peptide which detects the expression or function of protein synthesized or secreted by tumors.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

SEA